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Long-term outcomes of patients with multivessel coronary artery disease presenting non-ST-segment elevation acute coronary syndromes

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Abstract

Background: *There is paucity of data concerning the optimal revascularization in patients with multivessel coronary artery disease (CAD) presenting non-ST-segment elevation acute coronary syndrome (NSTE-ACS). The aim was to evaluate long-term outcomes of patients with multivessel CAD presenting NSTE-ACS depending on the management after coronary angiography.*

Methods: *3,166 patients with NSTE-ACS hospitalized between 2006 and 2014 were screened. After exclusions, 1,342 patients were enrolled with multivessel CAD and were divided depending on their management after coronary angiography; the medical-only therapy group (n = 91), the percutaneous coronary intervention (PCI) group (n = 1,122), the coronary artery bypass grafting (CABG) group (n = 129). Propensity scores matching was used to adjust for differences in patient baseline characteristics.*

Results: *After propensity score analysis, 273 well-matched patients were chosen. Both before and after matching, patients treated with a medical-only therapy were burdened with the highest percentage of 24-month all-cause death and non-fatal MI in comparison to PCI and CABG groups, respectively. In the CABG group, ACS-driven revascularization rate was lowest. In the overall population, PCI (HR 0.33; 95% CI 0.20–0.53; p < 0.0001) and CABG (HR 0.54; 95% CI 0.31–0.93; p = 0.028) were independent factors associated with favorable 24-month prognosis. However, in a matched population only PCI was an independent predictor of long-term prognosis with a 63% decrease of 24-month mortality (HR 0.37; 95% CI 0.19–0.69; p = 0.0020).*

Conclusions: *In patients with multivessel CAD presenting with NSTE-ACS, medical-only management is related with adverse long-term prognosis in contrast to revascularization, which reduces 24-month mortality, especially among patients undergoing percutaneous intervention. Performance of PCI is an independent factor for improving long-term prognosis.* (Cardiol J 2019; 26, 2: 157–168)

Key words: non-ST-elevation myocardial infarction, percutaneous coronary intervention, coronary bypass grafts, multivessel coronary artery disease, long-term outcomes

Introduction

Multivessel coronary artery disease (CAD) is observed in 35–70% cases of non-ST-segment elevation acute coronary syndromes (NSTE-ACS) [1–4]. Moreover, multivessel CAD is one of the most common causes of higher risk for cardiovascular morbidity and mortality in this population [5, 6]. Although, an early invasive approach in patients with moderate-to-high risk is recommended, management of patients with confirmed multivessel CAD is controversial [7–9]. The guidelines suggest

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that the artery responsible for ischemia should be treated first [9, 10]. However, in the case of multivessel CAD, subsequent treatment strategies include percutaneous coronary intervention, (PCI), coronary artery bypass grafting (CABG) or medical-only therapy. Choice of treatment modality, completeness and optimal timing of revascularization (one- or multi-stage) of remaining lesions remains a contentious issue. Lack of detailed recommendations regarding optimal revascularization strategy is caused by a paucity of randomized trials and a small number of retrospective studies [11–14].

The main purpose of this study was to evaluate long-term outcomes of patients with multivessel CAD presenting NSTE-ACS. Therefore, an analysis was performed of clinical and angiographic status and the impact of treatment management on the incidence of 24-month all-caused death and identification of independent risk factors influencing the prognosis.

Methods

Study design

In this single-center prospective study, registry data of 3,166 consecutive patients with NSTE--ACS hospitalized from January 2006 to December 2014 were screened. Patients without invasive diagnostics during the acute phase of NSTE-ACS, with a history of CABG, with non-obstructive or single-vessel CAD were excluded from further analysis. Enrolled patients were divided into three groups depending on treatment after coronary angiography: medical-only therapy group — patients qualified for medical conservative treatment; PCI group — patients treated with PCI in the first instance; CABG group — patients treated CABG in the first instance.

The diagnosis and treatment of the study population were conducted in a highlyspecialized cardiology center with cardiac surgery facilities. Management of patients was based on current recommendations of the European Society of Cardiology (ESC) [9, 15, 16]. All patients qualified for invasive strategy have received acetylsalicylic acid and weight-adjusted unfractionated heparin. Coronary angiography was performed routinely from radial or femoral artery access depending on operator discretion. During invasive diagnostics, standard guidewires and catheters were used. After coronary angiography all decisions regarding method of treatment (medical management, PCI, CABG), in particular the use of stents, type of stent, type of cardiac surgery operation, number of grafts, periprocedural use of anticoagulants and antiplatelet drugs, and further revascularization were dependent on the decision of the operator or the Heart Team. In cases of recurrence of stenocardial symptoms associated with ST-T deviations, urgent coronary angiography was performed. Dual-antiplatelet therapy was endorsed for at least 12 months subsequent to hospitalization. Others drugs were prescribed in accordance with the ESC Guidelines [9, 15, 16]. The next stage of revascularization was routinely planned up to 3 months after index hospitalization. The adopted method of division into groups allowed the hybrid revascularization approach.

Data collecting and acquisition

Demographic, clinical and echocardiographic data regarding index hospital stay were collected by physicians and uploaded to the institutional database. Additionally, a retrospective analysis of coronary angiography, morphology and location of coronary artery lesions in all patients was conducted. 24-month follow-up data, including specific date of death, non-fatal myocardial infarction (MI) and acute coronary syndrome (ACS) driven revascularization was obtained from the official registry of the National Health Fund, guaranteeing complete data collection. Detailed data from further hospitalization planned within 3 month after discharge was also implemented to the institutional database. Follow-up data was available for whole study population.

This study was granted permission from the Institutional Review Board and University Bioethics Committee, and is in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments [17].

Definitions and endpoints

NSTE-ACS was diagnosed on the basis of (1) clinical presentation: i) prolonged (> 20 min) anginal pain at rest, ii) new onset (*de novo*) angina (Class II or III of the Classification of the Canadian Cardiovascular Society), iii) recent destabilization of previously stable angina with at least Canadian Cardiovascular Society Class III angina characteristics (crescendo angina), (2) the absence of ST-segment elevation consistent with an infarction of ≥ 2 mm in contiguous chest leads, ST-segment elevation of ≥ 1 mm in 2 or more standard leads, or a new left bundle branch block and (3) after exclusion of alternative causes of chest pain [9, 15, 16]. Subsequently, patients with NSTE-ACS were classified as having unstable angina (UA) or

non-ST-segment elevation myocardial infarction (NSTEMI) based on measured values of markers of myocardial necrosis in accordance with the Universal Definition of Myocardial Infarction [18]. Since 2009 high-sensitive cardiac troponin T was measured in the institutional central laboratory. Multivessel CAD was defined as hemodynamically significant stenosis in left main (LM) or in at least two major epicardial territories or in their major branches (left anterior descending [LAD], left circumflex or right coronary artery system) with a diameter ≥ 2.0 mm as determined by visual assessment with on-line quantitative coronary angiography using orthogonal views [19]. As hemodynamically significant ≥ 50% diameter stenosis in LM or proximal segment of LAD and ≥ 70% diameter stenosis in other segments were also considered. Angiographic success was defined as the achievement of a minimum stenosis diameter reduction to < 20% in the presence of TIMI flow 3 grade.

The primary outcome measure included the occurrence of 24-month all-cause death. The secondary endpoints were non-fatal recurrent myocardial infarction (MI), ACS-driven unplanned revascularization and stroke at 24 months. Non-fatal MI was defined as an ischemic event that met ESC/American College of Cardiology criteria for MI and were clearly clinically separate from the baseline ACS at the time of admission [18]. ACS-driven repeat revascularization was defined as additional, unplanned angioplasty or CABG, performed as an urgent procedure because of acute ischemic symptoms [19]. Stroke was defined as an ischemic event that was in accordance with European Stroke Organization guidelines [20].

Statistical analysis

Statistical analysis included a comparison of baseline, angiographic and procedural characteristics, and the incidence of cardiovascular events during 24-month follow-up. The analyzed variables are expressed as numbers and percentages. The distribution normality was verified using the Shapiro-Wilk test. Continuous variables were summarized using arithmetic mean with standard deviation (SD) for data following normal distribution or median with quartile 1 and 3 (Q1–Q3) for data demonstrating non-normal distribution. The analysis of variance (ANOVA) test for comparison of continuous parameters with normal distribution was performed, whereas the Kruskal-Wallis ANOVA rank test for parameters with non-normal distribution was used. Categorical variables were compared using the χ^2 test with the Pearson's modification or with the Yates correction if the expected number of observations was less than 5. All-cause mortality, non-fatal MI, ACS-driven revascularization and stroke in 24-month follow-up for all patients were analyzed using the Kaplan-Meier method with log-rank test. To minimize the confounding impact of risk factors affecting 24-month outcomes. A propensity score analysis was performed to adjust for differences in patient baseline characteristics. First, logistic regression was performed to score all patients according to treatment (medical-only therapy vs. PCI; medical-only therapy vs. CABG), used as covariates the clinical and procedural parameters that were clinically relevant for the endpoint: age (years), gender (male/female), diabetes mellitus, prior MI, ST-segment deviation, left ventricular ejection fraction, triple-vessel CAD and chronic total occlusion. In the next stage, analyses were performed on two matched groups (medical-only therapy vs. PCI and medical-only therapy vs. CABG), stratified into pairs to account for propensity score matching. The nearest neighbor matching was used. Both before and after propensity score matching, the Cox proportional hazards model was performed. Factors were analyzed by stepwise backward elimination ($p < 0.3$ for entry into the model, $p < 0.05$ to remain in the model). The independence of factors were verified by interactions testing. Results were summarized as hazard ratio (HR) with 95% confidence interval (CI). A two-sided p-value < 0.05 was considered significant. The STATISTICA 10 software (StatSoft Inc., Tulsa, Oklahoma) was used for all calculations.

Results

During an observation period from 2006 to 2014, a total of 3,166 patients with NSTE-ACS were analyzed (Fig. 1). After exclusions, among patients with multivessel CAD, in 91 patients medical-only treatment was implemented while in the remaining 1,251 patients revascularization was performed. Of these, 1,122 patients underwent PCI and 129 patients CABG. The average age of the study population was 66.9 ± 10.9 years, 68.0% were males, and the definitive diagnosis of MI was recognized in 64.2%. Baseline characteristics and results of additional testing of the study groups are summarized in Table 1. In general, the medical-only treatment group had the worst clinical profile with the highest GRACE score results. The post-hoc analysis showed that patients from

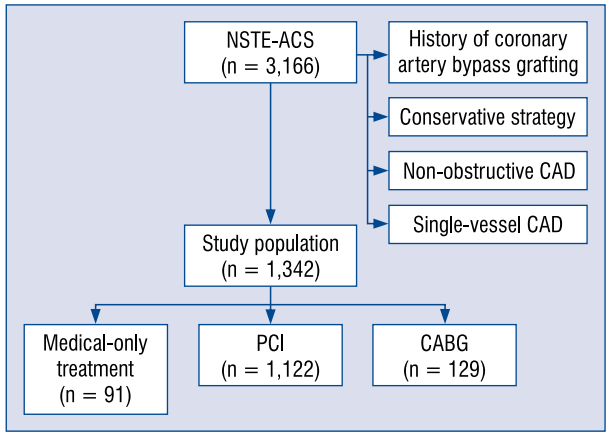

Figure 1. Study design; CABG — coronary artery bypass grafting; CAD — coronary artery disease; NSTE-ACS — non-ST-segment elevation acute coronary syndromes; PCI — percutaneous coronary intervention.

the PCI group in comparison with CABG group had significantly more frequently final NSTEMI diagnosis, higher troponin T ($p < 0.0001$), glucose level on admission ($p = 0.0029$), lower level of left ventricular ejection fraction ($p = 0.0033$), while less often arterial hypertension ($p = 0.012$) and peripheral artery disease ($p = 0.026$). Overall, the GRACE Risk in PCI in comparison with CABG group was higher ($p = 0.036$). Angiographic and procedural characteristics are presented in Table 2. Patients qualified to medical-only treatment and to cardiac surgery demonstrated more advanced severity of coronary disease when compared to patients treated with PCI. Overall, the rate of patients undergoing hybrid revascularization was 5.7% (6.1% in PCI group and 2.3% in CABG group). Approximately half of patients from CABG group underwent complete anatomic revascularization after 6-month from discharge, whereas in PCI group this proportion accounted for approximately one-third of patients.

After propensity score matching of the study population group, 273 patients were selected. Patients in medical-only therapy and PCI groups had lower left ventricular ejection fraction in comparison to CABG patients. Also, the overall GRACE score was higher in medical-only therapy than in CABG group. Left main disease was more frequent in medical-only therapy and CABG than in PCI group. The other differences in baseline clinical characteristics and angiography were reduced with nonsignificant p value.

Table 3 contains the in-hospital, early and long-term outcomes. Kaplan-Meier curves for

Table 1. Baseline characteristics of study population and matched cohort.

Factor	Study population (n = 1,342)			P	Matched group (n = 273)			P
	Medical-only treatment (n = 91)	PCI (n = 1,122)	CABG (n = 129)		Medical-only treatment (n = 91)	PCI (n = 91)	CABG (n = 91)	
Age (years ± SD)	68.4 ± 10.1	66.8 ± 10.5	66.8 ± 9.4	0.35	68.4 ± 10.1	68.6 ± 10.0	68.6 ± 8.8	0.93
Male	64.8%	67.7%	73.6%	0.29	64.8%	65.9%	68.1%	0.89
Diagnosis of NSTEMI	57.1%	67.6%	41.1%	< 0.0001	57.1%	54.9%	48.3%	0.46
Arterial hypertension	83.3%	75.3%	85.3%	0.011	83.3%	82.4%	87.9%	0.55
History of CAD	68.1%	57.0%	62.8%	0.065	68.1%	70.3%	70.3%	0.93
Prior MI	51.1%	39.0%	42.6%	0.051	51.1%	46.1%	53.8%	0.80
Prior PCI	29.6%	31.3%	20.2%	0.033	29.4%	35.2%	25.3%	0.35
Atrial fibrillation	12.8%	10.4%	10.1%	0.74	12.8%	16.5%	11.0%	0.54
Peripheral artery disease	21.6%	13.2%	20.2%	0.011	21.6%	28.6%	19.8%	0.34
Prior stroke	7.7%	7.2%	9.3%	0.67	7.7%	14.3%	13.2%	0.33
Diabetes mellitus	51.1%	37.3%	39.5%	0.024	51.1%	54.9%	50.6%	0.97
Diabetes mellitus insulin-treatment	22.7%	16.6%	18.6%	0.29	22.7%	19.8%	22.0%	0.88

Table 1 (cont.). Baseline characteristics of study population and matched cohort.

Factor	Study population (n = 1,342)			P	Matched group (n = 273)			P
	Medical-only treatment (n = 91)	PCI (n = 1,122)	CABG (n = 129)		Medical-only treatment (n = 91)	PCI (n = 91)	CABG (n = 91)	
Chronic kidney disease	11.8%	9.4%	5.4%	0.22	11.8%	10.0%	6.7%	0.42
Dyslipidemia	67.7%	67.5%	67.4%	0.99	67.7%	71.4%	74.7%	0.59
Obesity	29.5%	26.7%	18.6%	0.10	29.5%	34.1%	23.1%	0.26
COPD	9.9%	4.9%	2.3%	0.032	9.9%	6.6%	3.3%	0.20
History of cigarette smoking	45.1%	42.7%	43.4%	0.89	45.1%	35.2%	45.0%	0.30
Current smoking	18.7%	17.6%	17.0%	0.95	18.7%	22.0%	19.8%	0.85
Familiar history of MI	24.5%	22.6%	27.1%	0.49	24.5%	19.8%	24.2%	0.70
Chest pain*	89.0%	91.2%	90.7%	0.62	89.0%	90.1%	89.0%	0.96
Killip class III*	4.4%	2.4%	0.0%	0.11	4.4%	6.6%	0.0%	0.055
Killip class IV*	0.0%	1.4%	0.0%	0.21	0.0%	0.0%	0.0%	–
Heart rate* [bpm ± SD]	82 ± 19	78 ± 16	78 ± 15	0.13	82 ± 19	80 ± 14	80 ± 16	0.60
Systolic blood pressure* [mmHg ± SD]	143 ± 28	147 ± 29	147 ± 30	0.32	143 ± 28	147 ± 30	146 ± 33	0.76
Diastolic blood pressure* [mmHg ± SD]	84 ± 16	86 ± 16	85 ± 16	0.49	84 ± 16	84 ± 18	85 ± 17	0.83
ST-segment deviations*	57.6%	40.9%	44.7%	0.0061	57.6%	61.8%	51.5%	0.43
LBBB*	11.0%	6.1%	5.3%	0.20	11.0%	5.3%	7.4%	0.29
RBBB*	1.3%	5.6%	4.3%	0.21	1.2%	10.5%	4.4%	0.40
BMI [kg/m^2 ± SD]	28.5 ± 4.9	28.7 ± 4.8	28.4 ± 6.1	0.82	28.5 ± 4.9	28.3 ± 4.9	28.9 ± 6.8	0.73
Cardiac troponin T*# [ng/mL] (Q1–Q3)	0.11 (0.02–0.53)	0.10 (0.02–0.50)	0.05 (0.01–0.25)	0.011	0.11 (0.02–0.53)	0.10 (0.01–0.61)	0.09 (0.02–0.46)	0.94
Elevated cardiac troponin T*#	76.7%	77.9%	67.1%	0.078	76.7%	74.6%	79.7%	0.75
WBC* [thousand/μL] (Q1–Q3)	8.5 (6.8–11.4)	8.4 (6.9–11.4)	8.1 (6.8–9.6)	0.36	8.5 (6.8–11.4)	8.6 (6.5–10.6)	8.3 (7.0–10.4)	0.51
Hemoglobin* [mmol/L ± SD]	8.5 ± 1.0	8.5 ± 1.0	8.4 ± 0.9	0.59	8.5 ± 1.0	8.4 ± 1.0	8.3 ± 0.9	0.18
Glucose* [mmol/L] (Q1–Q3)	6.6 (5.8–9.3)	6.6 (5.5–8.6)	6.0 (5.0–8.1)	0.023	6.6 (5.8–9.3)	6.8 (5.6–9.4)	6.4 (5.0–8.8)	0.31
Serum creatinine* [μmol/L] (Q1–Q3)	88 (72–112)	84 (69–103)	86 (71–102)	0.51	88 (72–112)	84 (69–114)	91 (76–104)	0.67
eGFR* [mL/min/1.73 m^2] (Q1–Q3)	69 (49–86)	78 (58–97)	76 (58–95)	0.049	69 (49–86)	76 (54–100)	71 (56–86)	0.70
LVEF* [% ± SD]	38.0 ± 11.6	43.3 ± 10.4	46.1 ± 9.7	< 0.0001	38.0 ± 11.6	39.7 ± 11.2	43.5 ± 9.0	0.0028
LVEF < 35%*	47.6%	24.3%	14.4%	< 0.0001	47.6%	38.2%	16.7%	0.0002
GRACE scale [points] (Q1–Q3):	137 (115–154)	122 (103–143)	119 (97–133)	< 0.0001	137 (115–154)	133 (114–149)	129 (107–141)	0.035
> 140 points	46.9%	28.7%	15.1%	< 0.0001	46.9%	37.4%	27.6%	0.0093
109–140 points	31.0%	39.5%	50.0%	0.016	31.0%	40.7%	46.0%	0.074
≤ 108 points	22.1%	31.7%	34.9%	0.076	22.1%	22.0%	26.4%	0.70

*On admission; #Since 2009 high-sensitive cardiac troponin T was measured.
BMI — body mass index; CABG — coronary artery bypass grafting; CAD — coronary artery disease; COPD — chronic obstructive pulmonary disease; eGFR — estimated glomerular filtration rate; LBBB — left bundle branch block; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction; PCI — percutaneous coronary intervention; Q1–Q3 — quartile 1 and quartile 3; RBBB — right bundle branch block; SD — standard deviation; WBC — white blood cells

Table 2. Angiographic and procedural characteristics of study population and matched cohort.

Factor	Study population (n = 1,342)			P	Matched group (n = 273)			P
	Medical-only treatment (n = 91)	PCI (n = 1,122)	CABG (n = 129)		Medical-only treatment (n = 91)	PCI (n = 91)	CABG (n = 91)	
Triple-vessel CAD	52.0%	39.1%	59.7%	< 0.0001	52.0%	60.4%	54.9%	0.56
LM CAD	25.2%	8.8%	34.9%	< 0.0001	25.2%	7.7%	33.0%	0.0001
Chronic total oclussion	70.4%	45.2%	49.6%	< 0.0001	70.4%	71.4%	60.4%	0.22
PCI during initial hospitalization	–	99.2%	3.7%	< 0.0001	–	98.9%	–	–
Drug eluting stent	–	27.7%	–	–	–	34.4%	–	–
Angiographic success	–	91.3%	–	–	–	88.9%	–	–
Performed PCI after discharge	–	23.4%	2.3%	< 0.0001	–	16.5%	1.1%	0.0001
CABG during initial hospitalization	–	–	37.9%	–	–	–	31.9%	–
Performed CABG after discharge	–	6.1%	62.1%	< 0.0001	–	9.9%	68.1%	< 0.0001
Time from admission to first procedure [days] (Q1–Q3)	–	1 (1–1)	29 (11–49)	< 0.0001	–	1 (1–2)	28 (10–46)	< 0.0001
Complete revascularization	–	34.1%	51.9%	< 0.0001	–	20.9%	51.6%	< 0.0001

CABG — coronary artery bypass grafting; CAD — coronary artery disease; LM — left main; PCI — percutaneous coronary intervention; Q1–Q3 — quartile 1 and 3

study groups are presented in Figure 2. A total percentage of 12- and 24-month all-cause death in the overall study population was 12.8% and 18.7%, respectively. Patients treated with medical-only therapy were burdened with the highest percentage of 12- and 24-month all-cause death. Moreover, the highest rate of non-fatal MI in those patients was observed. In the CABG group, ACS-driven revascularization rate was the lowest. After propensity score matching, there were no differences in the incidence of 12-month events between analyzed groups. At 24 months, the medical-only treatment was associated with the highest occurrence of all-cause death and non-fatal MI, while in PCI group had the highest rate of ACS-driven revascularization.

The Cox proportional hazards model before (A) and after (B) propensity score matching is presented in Figure 3. In the study population, PCI and CABG were independent factors of improved 24-month prognosis. However, in matched population only PCI was an independent predictor of 24-month prognosis with reduction of 24-month mortality by 63%.

Discussion

The vast majority of contemporary studies comparing treatment strategy of multivessel CAD were performed in patients with stable angina [21––23]. Multicenter, randomized trials comparing PCI to CABG, encompassed from 13% to 91% patients with UA or recent MI [22]. In NSTE-ACS population, except for one single-center trial comparing an optimal timing of staged multivessel intervention [13], to date no prospective randomized clinical trial has been conducted to evaluate the treatment modality of multivessel CAD. Moreover, there is only a limited number of data obtained from one subanalysis of randomized trial and few retrospective studies [11, 12, 14, 24–26]. The optimal treatment method in overall as well as in particular subgroups of patients with NSTE-ACS is unclear. Therefore, the decision to conduct an assessment of treatment of multivessel CAD in real-world patients presenting with NSTE-ACS was undertaken.

In the present study comprising 3,166 patients with NSTE-ACS, the percentage of multivessel CAD without prior CABG was more than 42%. The present results are similar to those previously reported for NSTE-ACS patients, where occurrence of multivessel CAD ranged from 35% to 70% [1–4]. Also, baseline clinical and angiographic characteristics of the patients appears to be

Table 3. In-hospital, 30-day, 12-month and 24-month outcomes of study population and matched cohort.

Factor	Study population (n = 1,342)			P	Matched group (n = 273)			P
	Medical-only treatment (n = 91)	PCI (n = 1,122)	CABG (n = 129)		Medical-only treatment (n = 91)	PCI (n = 91)	CABG (n = 91)	
In-hospital outcomes:*								
All-cause death	5.5%	2.8%	3.9%	0.29	5.5%	4.4%	4.4%	0.92
Non-fatal MI	0.0%	1.3%	0.8%	0.51	0.0%	0.0%	1.1%	0.37
TVR#	0.0%	2.6%	0.0%	0.065	0.0%	3.3%	0.0%	0.48
Stroke	1.1%	0.4%	2.8%	0.0046	1.1%	1.1%	3.3%	0.44
Cardiogenic shock	0.8%	2.9%	0.0%	0.093	1.1%	2.2%	0.0%	0.36
Pulmonary edema	8.7%	4.5%	0.0%	0.0086	8.7%	8.7%	1.1%	0.046
Blood transfusion	4.4%	5.5%	3.7%	0.63	4.4%	8.8%	3.3%	0.23
Cardiac arrest	5.5%	3.4%	0.9%	0.22	5.5%	4.4%	0.0%	0.090
30-day:								
All-cause death	11.0%	4.0%	4.6%	0.0028	11.0%	4.4%	5.5%	0.098
Non-fatal MI	2.2%	2.3%	1.7%	0.94	2.2%	1.1%	1.1%	0.78
ACS-driven revascularization	1.1%	3.9%	0.0%	0.028	1.1%	3.3%	0.0%	0.17
Stroke	3.3%	0.4%	2.8%	0.0005	3.3%	1.1%	3.3%	0.82
12-month:								
All-cause death	25.3%	11.7%	11.1%	0.0010	25.3%	14.3%	14.3%	0.083
Non-fatal MI	14.3%	8.3%	4.6%	0.025	14.3%	12.1%	4.4%	0.070
ACS-driven revascularization	8.8%	10.1%	1.7%	0.019	8.8%	14.3%	4.4%	0.068
Stroke	4.4%	1.7%	4.6%	0.034	4.4%	3.3%	4.4%	0.91
24-month:								
All-cause death	42.1%	16.5%	20.5%	< 0.0001	42.1%	23.0%	22.0%	0.0041
Non-fatal MI	19.3%	11.1%	4.7%	0.0035	19.3%	14.9%	5.5%	0.020
ACS-driven revascularization	12.5%	12.7%	4.7%	0.031	12.5%	19.5%	4.4%	0.0080
Stroke	3.4%	3.0%	7.1%	0.062	4.4%	3.4%	7.7%	0.31

*during index hospitalization; ACS — acute coronary syndrome; CABG — coronary artery bypass grafting; MI — myocardial infarction; PCI — percutaneous coronary intervention; TVR — target vessel revascularization

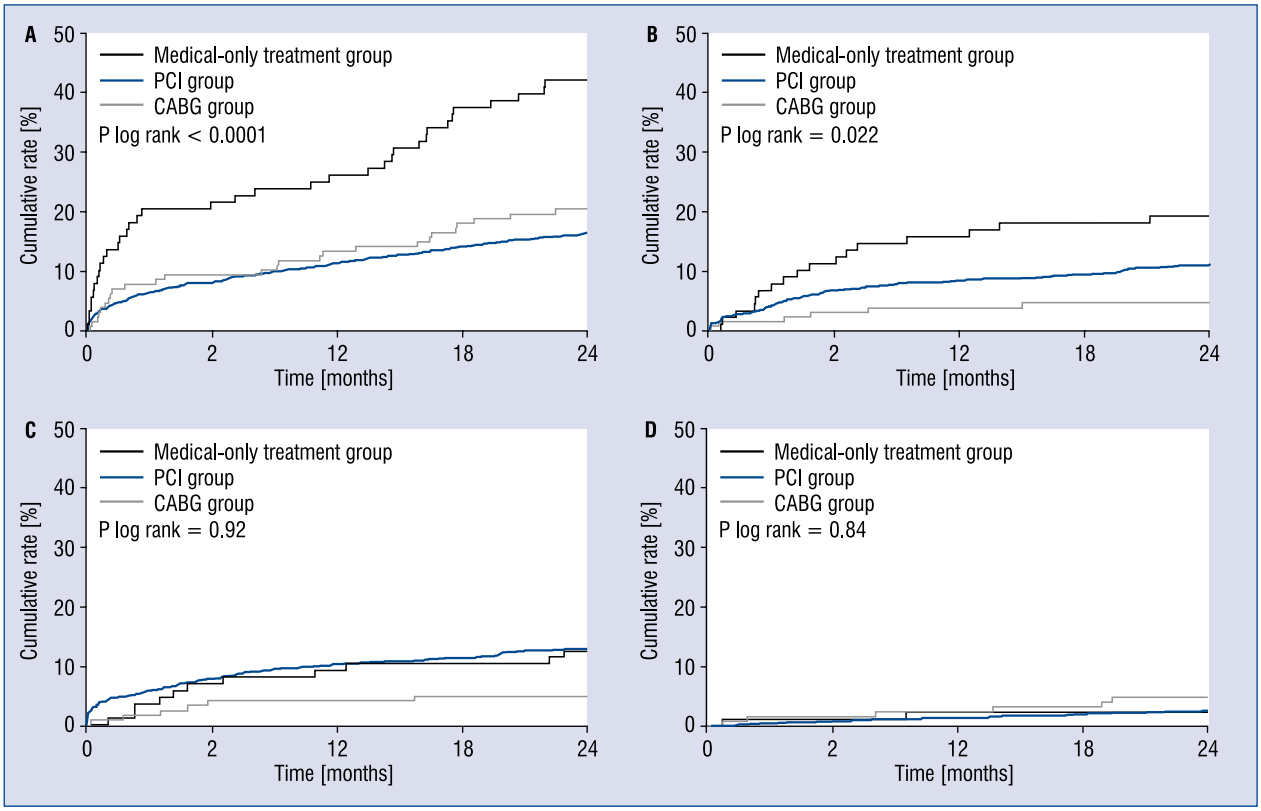

Figure 2. Kaplan-Meier survival curves for 24-month rates of all-cause death (**A**), non-fatal myocardial infarction (**B**) acute coronary syndromes-driven revascularization (**C**) and stroke (**D**) in study groups; CABG — coronary artery bypass grafting; PCI — percutaneous coronary intervention.

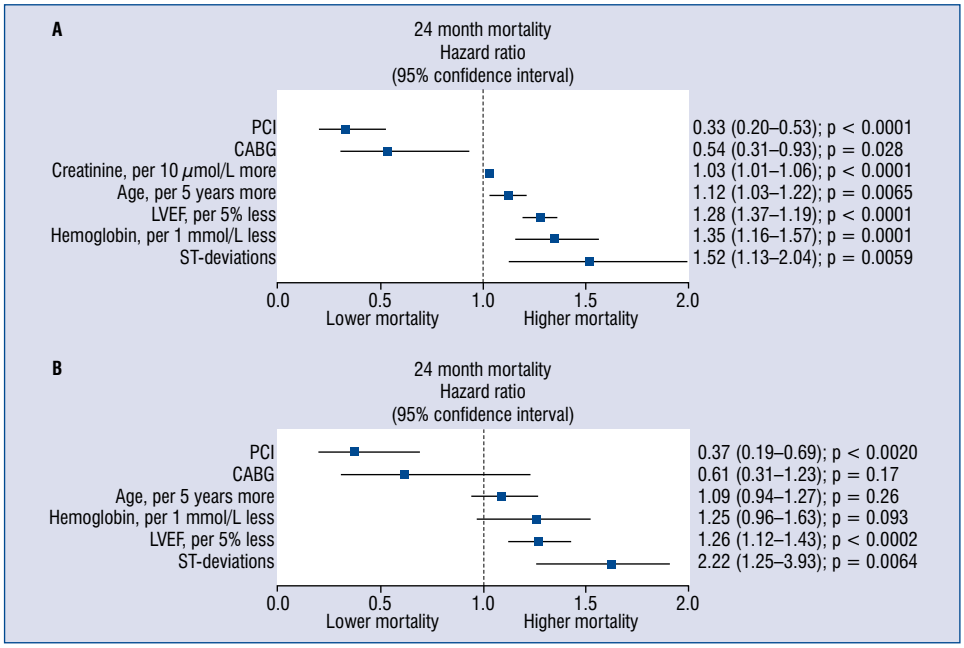

Figure 3. Forest plot of independent predictors of 24-month all-cause mortality in the study population (**A**) and in a matched cohort (**B**); CAD — coronary artery disease; CI — confidence interval; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention.

comparable to other registries, this demonstrates a good reflection of the present patients to the general population of NSTE-ACS [11, 12, 25]. In this study, patients treated invasively constituted less than 84%, surgical treatment was performed in 10% and in remaining patients the medical-only treatment was implemented. Gierlotka et al. [27] found that the rates of revascularization among Polish patients with NSTEMI shows an upward trend with contemporary use of PCI in more than 55%, and CABG in more than 10% patients. In subanalysis of ACUITY trial, designed to compare two methods of revascularization in multivessel CAD, patients undergoing PCI accounted for 78%, while CABG group consisted of 22% of study population [14]. Also, in other studies PCI was the most common method of treatment for multivessel CAD in NSTE-ACS [24–26, 28].

Early and long-term outcomes in the present analysis have shown that patients treated conservatively after coronary angiography are characterized by the worst prognosis. This result is intelligible in terms of current state of the art of management in NSTE-ACS [9, 29]. Qualification for medical-only treatment after diagnostic coronary angiography may be result of anatomical infeasibility of revascularization (i.e. rates of chronic total occlusions) and/or severe clinical status of patients [30]. The long-term outcomes were similar in PCI and CABG groups, except for higher frequency of ACS-driven revascularization in PCI group. There were no differences in the occurrence of stroke. In virtually all clinical trials, CABG was associated with higher rates of stroke in comparison with PCI [31]. The results of ACUITY trial showed that invasive treatment may be associated with lower incidence of non-fatal periprocedural MI, stroke and major bleeding, while CABG with lower occurrence of recurrent ischemia [14]. After propensity score matching analysis, early and long-term mortality in patients treated with PCI was similar to CABG group. However, an insignificant, but numerically higher incidence of the composite endpoint (25% vs. 19%; $p = 0.053$) was observed, which was mainly driven by a meaningfully higher percentage of unplanned repeat revascularization (12% vs. 0.2%; $p < 0.001$). A similar correlation demonstrating comparable efficacy of PCI and CABG in NSTE-ACS has been demonstrated in the issue of unprotected LM coronary artery [32, 33], a proximal segment of LAD [34] and in patients with multivessel CAD and diabetes mellitus [35]. On the other hand, in the MILESTONE Registry, immediate PCI was associated with lower long-term mortality risk compared with surgical revascularization, especially in subgroups at high clinical risk [26]. Importantly in the present study, after adjusting for factors from baseline and angiographic characteristics, the performance of PCI was an independent predictor of improved prognosis in 24-month follow-up. These meaningful outcomes are in accordance with the expert opinions that after identification a culprit vessel during coronary angiography, PCI should be the first choice procedure in the treatment of NSTE-ACS. After PCI of culprit vessel, further decisions regarding revascularization of non-ischemia-related vessels should be carried out after Heart Team consultation or based on the locally adopted proceedings protocols. PCI should also be recommended in the case of an occurrence of multiple lesions responsible for the manifestation of NSTE-ACS [36].

It is well documented that most benefits from an invasive strategy and subsequent PCI refers to patients undergoing intervention respectively in 24 (high risk) or 72 (moderate risk) hours from admission to hospital [9]. However, another important issue in multivessel CAD is optimal timing of revascularization in vessels other than the culprit vessel. There is widespread agreement of experts that in stable clinical status after intervention in the artery responsible for NSTE-ACS, treatment decisions regarding other stenosed vessels may be based on recommendations for stable CAD. In patients with severe, multivessel CAD, the preferred modality of treatment recommended by ESC is CABG. Nevertheless, outcomes of SYNTAX and EXCEL trials indicate that, the use of PCI as an alternative to cardiac surgery may be applied in patients with low-to-moderate SYNTAX score [21, 37, 38]. In the present study, more than a quarter of patients in PCI group was scheduled for the next stage of revascularization after discharge, whereas in 62% patients of CABG group, the operation was performed during further hospitalization. The results of retrospective studies and their meta-analyzes suggest that performing multivessel PCI during index hospitalization in patients presenting with NSTE-ACS may improve a long-term prognosis [11, 12]. Sardella et al. [13] in SMILE Trial has demonstrated that one-stage multivessel PCI is superior to postponed intervention. Due to a lack of randomized trials, optimal time frames of performance of CABG in NSTE-ACS patients are unclear. In accordance with expert consensus and results of clinical registries, CABG should be implemented after 48–72 hours after performance of culprit vessel PCI, except for patients

with ongoing myocardial ischemia, hemodynamic instability or very-high-risk coronary anatomy when there should be no delay with an operation [39]. However, the final decision should be taken by the Heart Team on the basis of clinical status and severity of CAD.

The previous data indicate that more complete revascularization of multivessel CAD may be associated with lower frequency of adverse events, particularly repeat urgent revascularization when compared to treatment limited only to the artery responsible for NSTE-ACS manifestation [11, 12]. Herein was found that the percentage of patients who underwent complete revascularization within 6 months after diagnosis of NSTE-ACS was more than 34% in PCI group and more than 50% in the CABG group. Similarly, a meta-analysis of retrospective studies proved that performance of multivessel PCI results in a reduction of long-term composite endpoint, mainly due to lower incidence of ischemia-driven revascularization. Data above indicate the need for complete revascularization in patients with multivessel CAD, if anatomical factors and the clinical condition allows.

Limitations of the study

This study was a single-center, retrospective study with potential selection biases. After coronary angiography, the further treatment decisions to perform PCI or CABG was at the operator or Heart Team discretion. The results of SYNTAX score and EuroScore were not available. Multivariate analysis may be biased because of the potential effect of confounding predictors that were not accessible in this database. A longer period of follow-up is required for more complete evaluation of PCI and CABG treatment.

Conclusions

In summary, presented results indicate that more than 90% of patients with multivessel CAD in the course of NSTE-ACS underwent coronary revascularization, of which the vast majority were treated by percutaneous intervention. The highest morbidity, risk and severe of CAD was observed in patients qualified for medical-only treatment. Also, medical-only management was related worse long-term prognosis in contrast to revascularization, which reduces 24-month mortality. In addition to known factors associated with higher mortality, the use of PCI is an independent factor for improving prognosis of 24-month follow-up. Optimal revascularization method in multivessel CAD and NSTE-ACS patients requires multicenter and randomized trials in the future.

Conflict of interest: None declared

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